510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR § 807.92.

The assigned 510(k) number is: K100951

Submitted By: MEDTOX® Diagnostics, Inc.
1238 Anthony Road
Burlington, North Carolina 27215

Contact Person: Phillip Hartzog, Ph.D.
Director, Research & Development
Phone: 336-226-6311, ext. 2863
Fax: 336-229-4471

OCT 18 2010

Date Prepared: September 22, 2010

Proprietary Name: MEDTOX® Buprenorphine Test

Common Name: Buprenorphine test

Classification Names: Buprenorphine test system

The applicant test system regulatory classification is Class II; the Classification Panel is Clinical Toxicology (91) and Clinical Chemistry (75). Regulatory information applicable to the test system is provided below:

CFR Section	Product Code
862.3650, Opiate Test System (Buprenorphine)	DJG

Predicate Device: Acon BUP One Step Buprenorphine Test (K060466)

Description of the Device
The MEDTOX® Buprenorphine Test is a rapid, single use, one-step qualitative immunochromatographic screening assay for the detection of Buprenorphine and its metabolites in human urine.

Intended Use

The MEDTOX Buprenorphine Test uses immunochromatographic test strips for the rapid, qualitative detection of buprenorphine and its metabolites in human urine. It is intended for prescription use only. The MEDTOX Buprenorphine Test is not for over-the-counter sale. It is not intended for use in point-of-care settings.

MEDTOX Buprenorphine detects buprenorphine and its metabolites at the following cutoff concentrations:

BUP Buprenorphine (Buprenorphine) 10 ng/mL

The MEDTOX Buprenorphine Test provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Liquid chromatography/tandem mass spectrometry (LC/MS/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any test result.

Discussion of Technological Characteristics:

Similarities and differences to predicate device
Both the MEDTOX® Buprenorphine Test and the predicate test are used to detect the presence of buprenorphine and its metabolites in human urine. In both systems, a urine sample is added to the test device and allowed to react for a specified period of time, after which the test device is read and interpreted visually. Both the MEDTOX® Buprenorphine Test and predicate test devices are rapid single use disposable devices that use immunochromatographic lateral flow technology. Both the MEDTOX®

Buprenorphine Test and predicate test devices utilize gold-conjugated reagents to generate the reddish-purple test and control lines, which are read visually.

Sample is applied to the MEDTOX® Burpenorphine Test by tilting a urine cup containing urine, while sample is applied to the predicate test by dipping the specified end of the test strip into the urine sample. The MEDTOX® Burpenorphine Test has a read time window of 5 to 15 minutes, while the predicate test read time window is 5 to 10 minutes.

Overall characteristics of the MEDTOX® Buprenorphine Test and the predicate device are summarized in Table 1 below:

Similarities		
Item	Indications	Predicate, K060644
Intended Use	Determines a preliminary qualitative positive or negative result for the presence of buprenorphine and its metabolites in human urine.	Same
Cutoff	10 ng/mL	Same
System Procedure	Sample is added to a single use test strip, which is then read visually.	Same
Measurement Method	Visual	Same
Results	Provides preliminary negative, non-negative and invalid visual test results.	Same
Differences		
Item	Indications	Predicate, K060644
Sample application	Urine is applied to strip by tilting urine cup	Strip is dipped into urine for a minimum of 5 seconds
Assay Time	Test is read between 5 and 15 minutes	Test is read between 5 and 10 minutes

Table 1. Comparison of Similarities and Differences for the MEDTOX® Buprenorphine Test and the predicate device.

The following laboratory performance studies were conducted to determine the substantial equivalence of the MEDTOX® Buprenorphine Test to the predicate device. The studies included confirmation of the buprenorphine concentration by LC/MS/MS methods:

Discussion of Non-Clinical Tests Performed for Determination of Substantial Equivalence:
The following laboratory performance studies were conducted to determine the substantial equivalence of the MEDTOX® Buprenorphine Test to the predicate:

Performance of the MEDTOX® Buprenorphine Test around the specific cutoff for Buprenorphine (10 ng/mL) was evaluated by testing standard drug solutions diluted in drug-free urine in triplicate on 5 different intervals by 3 in-house operators (45 determinations for each level). Drug free urine was also tested on each interval. The results were interpreted at 5 minutes and are summarized in Table 2 below:

Table 2. Sensitivity/Precision/Distribution of Random Error

Buprenorphine (10 ng/mL)				
Sample Concentration (ng/mL)	**% of Cutoff**	**Number of Observations**	**# Neg**	**# Pos**
0	Neg	45	45	0
2.5	25%	45	45	0
5.0	50%	45	45	0
7.5	75%	45	28	17
12.5	125%	45	4	41
15.0	150%	45	0	45

Analytical specificity (cross reactivity and interference) data are summarized below.

Related Compounds and Cross Reactants

The metabolites and reacting compounds shown in Table 3 below were evaluated on the MEDTOX® Buprenorphine Test for interference or cross reactivity with Buprenorphine. Reference standards for the various metabolites and compounds were prepared in negative urine samples. Results are expressed as the approximate minimum concentration required to produce a positive result in the indicated assay. Compounds that reacted with the test are listed first, and related compounds that did not react with the highest concentration tested are listed second as Negative at 100,000 ng/mL (or highest level tested). The "% Cross-Reactive" values were calculated from the cut-off level for the calibrator used for each test (approximate 50% positive rate) divided by the lowest reported level found to react in the same test (greater than 66% positive rate). Three different lots were tested and identical results were obtained. The non-reacting opiate compounds were also tested following the study of M.L. Smith, et. al.[1] Drug free urine samples were spiked with buprenorphine to the targeted concentrations of 5 ng/mL (50% of the cutoff) and 15 ng/mL (150% of the cutoff). 100 µg/mL of the non-reactive opiate compounds were then added to the preparation and assayed by MEDTOX Buprenorphine Test. Samples were evaluated in triplicate by in-house operators. None of the non-reactive opiate listed in the following table affected the expected results.

Table 3. Related Compounds and Cross Reactants in the MEDTOX® Buprenorphine Test

Buprenorphine (BUP) *(Buprenorphine, 10 ng/mL)*		
Compound	**Result**	**% Cross-Reactive**
Buprenorphine-glucuronide	Positive at 7.5 ng/mL	133%
Norbuprenorphine	Positive at 50 ng/mL	20%
Norbuprenorphine-glucuronide	Positive at 75 ng/mL	13%
Codeine	Negative at 100,000 ng/mL	None Detected
Diacetylmorphine	Negative at 100,000 ng/mL	None Detected
Hydrocodone	Negative at 100,000 ng/mL	None Detected
Hydromorphone	Negative at 100,000 ng/mL	None Detected
Levorphanol	Negative at 50,000 ng/mL	None Detected
6-Monoacetylmorphine	Negative at 100,000 ng/mL	None Detected
Morphine	Negative at 100,000 ng/mL	None Detected
Nalbuphine	Negative at 100,000 ng/mL	None Detected
Naloxone	Negative at 100,000 ng/mL	None Detected
Naltrexone	Negative at 100,000 ng/mL	None Detected
Norcodeine	Negative at 100,000 ng/mL	None Detected
Noroxycodone	Negative at 100,000 ng/mL	None Detected
Noroxymorphone	Negative at 100,000 ng/mL	None Detected
Oxycodone	Negative at 100,000 ng/mL	None Detected
Oxymorphone	Negative at 100,000 ng/mL	None Detected
Thebaine	Negative at 100,000 ng/mL	None Detected

Interference Data

pH and Specific Gravity:

The MEDTOX® Buprenorphine Test was assayed with four negative clinical samples with pH values of 5.0, 6.0, 7.0, and 8.0 ± 0.1. Each sample was assayed in triplicate. The pH samples were fortified with buprenorphine to the concentrations of 5 ng/mL and 15 ng/mL. All the pH levels gave negative results when fortified to 5 ng/mL, and all pH levels gave positive results when fortified to 15 ng/mL.

The MEDTOX® Buprenorphine test was assayed with three samples with specific gravity values of 1.003, 1.015 and 1.030 ± 0.001. Each sample was assayed in triplicate. The specific gravity samples were fortified with buprenorphine to the concentrations of 5 ng/mL and 15 ng/mL. All the specific gravity levels gave negative results when fortified to 5 ng/mL, and all specific gravity levels gave positive results when fortified to 15 ng/mL.

Non-Crossreactive Endogenous Compounds:
The endogenous compounds were tested following the study of M.L. Smith, et. al.[1] Drug free urine samples were spiked with buprenorphine to the targeted concentrations of 5 ng/mL (50% of the cutoff) and 15 ng/mL (150% of the cutoff). Most of the compounds were evaluated for interference of the MEDTOX Buprenorphine Test at 100 µg/mL (albumin was evaluated at 20 mg/mL and bilirubin was evaluated at 200 µg/mL). Samples were evaluated in triplicate by in-house operators. None of the endogenous compounds listed below affected the expected results.

Acetaldehyde	Creatinine	Sodium Chloride
Acetone	Epinephrine	Tetrahydrocortisone
Albumin, Human	β-Estradiol	d,1-Thyroxine
Ascorbic acid	Estriol	Uric Acid
Bilirubin	Glucose Std. Solution	
Cholesterol	Hemoglobin, Human	

Common Drugs:
Drug free urine samples were spiked with buprenorphine to the targeted concentrations of 5 ng/mL (50% of the cutoff) and 15 ng/mL (150% of the cutoff). 100 µg/mL of the common drugs were then added to the preparation and assayed by MEDTOX® Buprenorphine test. Samples were evaluated in triplicate by in-house operators. None of the common drugs listed in the following table affected the expected results.

Table 4. Common Drugs Evaluated with the MEDTOX® Buprenorphine Test

Acetylsalicylic Acid	Chlorpheniramine	Ibuprofen
Acetaminophen	Cocaine	Morphine
Amitriptyline	Dextromethorphan	Phenobarbital
Brompheniramine maleate	Diphenylhydantoin	d-Pseudoephedrine
Caffeine	Doxylamine	Rifampin
Carbamazepine	Fluoxetine	Salicylic Acid
		Vancomycin

Discussion of Clinical Tests Performed for Determination of Substantial Equivalence:
The accuracy of the MEDTOX® Buprenorphine Test was evaluated by assaying a panel of blind coded clinical urine samples containing varying concentrations of buprenorphine and its metabolites, and comparing the results with LC/MS/MS results. The samples were obtained from MEDTOX® Laboratories and are representative of intended population of clinical samples. Samples were screened with the CEDIA immunoassay system(Buprenorphine cutoff of 5ng/ml). Samples are stratified into the five following groups: (1) Negative samples were screened negative by CEDIA immunoassay system, 10% of which were confirmed negative by LC/MS/MS; (2) Near Cutoff Negative samples that fell between 50% of the cutoff concentration and the cutoff concentration; (3) Near Cutoff Positive samples that fell between the cutoff concentration and 150% of the cutoff concentration; and (4) High Positive samples that were greater than 150% of cutoff concentration. Concentrations measured by LC/MS/MS included the test-specific analytes (buprenorphine and norbuprenorphine) found in the sample. The testing was performed by in-house operators according to the package insert. The results were interpreted visually at five (5) minutes. No false positives were observed in the absence of drug. The tests were read at both 5 minutes and 15 minutes and identical results were obtained. The results are summarized in Table 5 below.

Table 5.
MEDTOX® Buprenorphine Test vs Stratified LC/MS/MS Values

DRUG	MEDTOX® Buprenorphine Test	No Drug	Near Cutoff Negative (between -50% and cutoff)	Near Cutoff Positive (Between cutoff and +50%)	High Positive (greater than +50%)	% Agreement
BUP (10 ng/mL)	Positive	0	3	8	72	100%
	Negative	70	4	0	0	96.1%

For samples giving preliminary positive results below the cutoff, the assayed values are detailed in Table 6 below:

Table 6. ACCURACY/SUMMARY of DISCORDANT RESULTS

MEDTOX® Buprenorphine Test (10 ng/mL)	LC/MS/MS Value (Drug or Metabolite, ng/mL)
positive	total buprenorphine at 5 ng/mL
positive	total buprenorphine at 7 ng/mL
positive	total buprenorphine at 9 ng/mL

Conclusions:

The MEDTOX® Buprenorphine Test has the same intended use and similar technological characteristics as the predicate device. Moreover, bench testing contained in this submission demonstrates that any differences in their technological characteristics do not raise any new issues of safety or effectiveness. Thus, the MEDTOX® Buprenorphine Test is substantially equivalent to the predicate device.

Reference

1. Smith, M.L., Shimomura, E.T., Summers, J., Paul, B.D., Nichols, D., Shippee, R., Jenkins, A.J., Darwin, W.D., and Cone, E.J. Detection Times and Analytical Performance of Commercial Urine Opiate Immunoassays Following Heroin Administration, Journal of Analytical Toxicology. Volume 24:7. October 2000, pages 522-529.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food & Drug Administration
10903 New Hampshire Avenue
Building 66
Silver Spring, MD 20993

OCT 18 2010

Medtox Diagnostics Inc.
c/o Phillip Hartzog
Director, Research and Development
1238 Anthony Road
Burlington, NC 27215

Re: k100951
Trade Name: Medtox Buprenorphine Test
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate Test System
Regulatory Class: Class II
Product Codes: DJG
Dated: September 23, 2010
Received: September 24, 2010

Dear Dr. Hartzog:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Courtney Harper, Ph.D.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

K100951

510(k) Number (if known): K100951

OCT 18 2010

Device Name: MEDTOX® Buprenorphine Test

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Prescription Use __X__ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

K100951